

Applicant: Timothy Bestor  
Serial No.: 09/051,013  
Filed: October 9, 1998  
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**REMARKS**

Claims 48-56 are pending in the subject application. Applicant has amended claims 48-53 to introduce certain formatting changes. Applicant maintains that the amendments to the claims do not introduce an issue of new matter. Accordingly, claims 48-56 will still be pending and under examination in the subject application upon entry of this Amendment.

Applicant respectfully requests that, in view of the remarks made herein, the Examiner withdraw the outstanding objections and rejections.

**The November 12, 2004 Advisory Action**

In the November 12, 2004 Advisory Action, the Examiner stated that applicant's October 14, 2004 Amendment would not be entered under 37 C.F.R. 1.121. Applicant maintains that this Preliminary Amendment is in compliance with 37 C.F.R. 1.121, and respectfully requests that it be entered.

In the Advisory Action, the Examiner also stated that applicant's October 14, 2004 Amendment, if entered, would appear to overcome the rejection under 35 U.S.C. §112, second paragraph made in the July 14, 2004 Office Action.

However, the Examiner also stated that the written description and enablement rejections under 35 U.S.C. §112, first paragraph, would be maintained for the reasons of record. Applicant has reiterated below the arguments made in his

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October 14, 2004 Amendment. With respect to the rejections under 35 U.S.C. §112, first paragraph, applicant intends to soon pursue this matter further with the Examiner in the hope of furthering prosecution of this application.

### **Objections**

The Examiner objected to claims 50 and 51 in the recitation of "LexA site" in line 3 of claim 50 and in the recitation of "LexA DNA site" in lines 2-3 of claim 51. In response, applicant respectfully points out that claims 50 and 51 have been amended to maintain consistency in the claims, overcoming the objection thereof. The Examiner also objected to claims 52 and 53 as being grammatically incorrect in the recitation of "and Spiroplasma DNA methyltransferase." In response, applicant respectfully points out that claims 52 and 53 have been amended to correct the grammatical error, overcoming the objection thereof.

### **Rejection under 35 U.S.C. §112, Second Paragraph**

The Examiner rejected claims 48-56 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner stated that there is insufficient antecedent basis for the limitation "the DNA binding region of LexA" in claims 48 and 49 (claims 50-51 and 56 dependent therefrom) and insufficient antecedent basis for the limitation "the Lac operator sequence" in claims 52-55 (claim 56 dependent of 52 and 53).

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In response to the rejection of claims 48-56, applicant respectfully points out that claims 48-53 have been amended to provide sufficient antecedent basis for the limitations, thereby overcoming the objection thereof.

In view of the above remarks, applicant respectfully requests that the Examiner withdraw the rejection under 35 U.S.C. §112, second paragraph.

**Rejections under 35 U.S.C. §112, First Paragraph**

The Examiner rejected claims 48-56 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Applicant addresses the rejection as applied to newly amended claims 48-56.

In response to the Examiner's rejection of claims 48-56, applicant respectfully traverses for the reasons of record and for the additional reasons set forth below.

35 U.S.C. §112, first paragraph, states that "[t]he specification shall contain a *written description* of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same..." (emphasis added)

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Briefly, claims 48-51 provide a chimeric protein comprising a *Spiroplasma* DNA methyltransferase (*M.SssI* DNAMt) and a LexA DNA binding protein, wherein the LexA DNA-binding protein binds to a region of DNA ("LexA binding region"), and wherein the *M.SssI* DNAMt specifically methylates CpG sites adjacent to a DNA binding region of LexA and vectors encoding therefor. Claims 52-56 provide a chimeric protein comprising a LacI protein and *M.SssI* DNAMt, wherein the *M.SssI* DNAMt specifically methylates sites adjacent to a Lac operator sequence and vectors encoding therefor.

The claimed invention is based on applicant's *surprising* discovery that chimeric DNA methyltransferase-DNA binding proteins can selectively methylate CpG sites within the promoter of a gene and thus inhibit expression of the gene.

In support of the rejection, the Examiner asserts that the specification does not fully describe the genus of claimed chimeric proteins. The Examiner further asserts that the specification does not disclose the structure of the claimed genus of chimeric proteins because it fails to disclose the structure of at least one "necessary" component of the chimeric protein, i.e. a *mutant M.SssI* DNAMt or a DNA encoding same. The Examiner asserts that mutations in the *M.SssI* DNAMt "are an essential and critical feature of the claimed invention."

In response, applicant maintains that the specification provides written description for the subject matter claimed. Initially, applicant notes that the instant claims do not recite any language indicating that *mutated M.SssI* DNAMt is an

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essential or critical feature of the claimed chimeric proteins. The pages cited by the Examiner in support of his position are merely examples for obtaining one type of *M.SssI* DNAmT with an attenuated DNA binding activity and are not to be construed as limiting the instant invention to only mutated forms of *M.SssI* DNAmT. In fact, the specification at page 13, lines 3-15, explicitly defines DNA methyltransferase to include "wild type DNA methyltransferase, [or] a naturally occurring DNA methyltransferase." Therefore, the instant invention is not solely directed to chimeric *mutant* DNA methyltransferase-DNA binding proteins, but rather to all embodiments of the claimed chimeric DNA methyltransferase-DNA binding proteins, generally.

To overcome the instant rejection, the specification must provide a representative number of such chimeric proteins. Applicant maintains that a representative number of examples have been set forth in the specification. Applicant directs the Examiner's attention to Example 7 on page 54, line 15 to page 56, line 18 and Figures 12-15. The example provides a working model of the claimed chimeric protein comprising a non-mutated DNA methyltransferase. The example further illustrates that chimeric DNA methyltransferase-DNA binding proteins can selectively methylate CpG sites in the vicinity of the recognition sequence of the DNA binding protein moiety and, taken together with the other teachings of the specification, is evidence that applicant was in possession of the claimed genus of chimeric proteins.

The Examiner also rejected claims 48-56 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which

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was not described in the specification in such a way as to allow one skilled in the relevant art to which it pertains to make and/or use the invention commensurate in scope with the claims.

In response, applicant respectfully traverses for the reasons of records and for the additional reasons set forth below.

The Examiner alleges that the specification fails to enable the broad scope of the claims. The Examiner further asserts that this lack of enablement arises from lack of written description regarding specific mutations that would produce a methyltransferase having the desired activity for use in the claimed chimeric protein.

However, as set forth above, the subject invention is not limited to chimeric proteins containing mutated forms of DNA methyltransferase. Rather, as defined in the specification, the instant chimeric proteins include those comprising wild-type or naturally occurring DNA methyltransferase. As the Examiner concedes on page 9 of the instant Final Office Action, "sequences of *naturally-occurring Spiroplasma* DNA methyltransferase, LexA protein, and LacI protein and methods for fusing two known nucleic acid sequences to generate a functional fusion protein were known in the art at the time of the invention." (emphasis added). Therefore, given that such sequences and methods were readily available and known in the art, one skilled in the art would not have to perform undue experimentation in order to make and use the claimed invention, i.e. a chimeric protein comprising a DNA methyltransferase and a DNA binding protein.

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In view of the above remarks, applicant respectfully maintains that claims 48-56 satisfy the requirements of 35 U.S.C. §112, first paragraph.

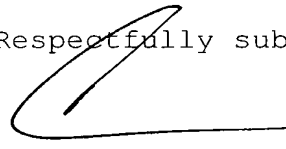
**Summary**

Applicant maintains that the claims pending are in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone conference would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the \$395.00 RCE filing fee, is deemed necessary in connection with the filing of this Preliminary Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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